

## AMENDMENT

### In the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application.

1. (Currently Amended): A method for genetically altering a subject patient whose thymus has been at least in part deactivated, comprising the steps of:  
genetically modifying cells, ~~wherein the cells are selected from the group~~  
consisting of hematopoietic stem cells (HSC), HSC, lymphoid progenitor cells, myeloid progenitor cells, epithelial stem cells, and combinations thereof[[,]]; and  
~~delivering them~~ administering the cells to the patient[[,]] while the patient's thymus is undergoing reactivation by disruption of sex steroid-mediated signaling to the patient's thymus.
2. (Currently Amended): The method of claim 1, further comprising the step of ablating T cells in the patient ~~T-cell ablation~~ prior to ~~administration of~~ administering the genetically modified cells to the patient.
3. (Canceled)
4. (Currently Amended): The method of claim 3, wherein the patient is post-pubertal.
5. (Currently Amended): The method of claim 3, wherein the patient has or had a disease or treatment of a disease that at least in part deactivated the patient's thymus.

6. (Currently Amended): The method of claim 1<sub>4</sub> wherein the cells are from the patient.
7. (Currently Amended): The method of claim 1<sub>4</sub> wherein the cells are not from the patient.
8. (Currently Amended): The method of claim 1<sub>4</sub> wherein the patient has a T cell disorder.
9. (Currently Amended): The method of claim 8<sub>4</sub> wherein the T cell disorder is caused by a condition selected from the group consisting of T cell functional disorder, HIV infection, and T cell leukemia virus infection.
10. (Currently Amended): The method of claim 9<sub>4</sub> wherein the cells are genetically modified ~~to inhibit infection of the cells by virus~~ in vitro with a vector construct encoding and expressing a gene product that inhibits replication of human immunodeficiency virus (HIV).
11. (Currently Amended): The method of claim 9<sub>4</sub> wherein the cells are genetically modified to inhibit replication of virus within T cells.
12. (Currently Amended): The method of claim 9<sub>4</sub> wherein the T cell disorder is caused by HIV infection.
13. (Currently Amended): The method of claim 12<sub>4</sub> wherein the cells are genetically modified to include a stably expressible polynucleotide selected from the group

consisting of a nef transcription factor gene, a gene that codes for a ribozyme that cuts HIV *tat* and/or *rev* genes, the trans-dominant mutant form of HIV-1 *rev* gene (RevM10), an overexpression construct of the HIV-1 *rev*-responsive element (RRE), and function fragments thereof.

14. (Currently Amended): The method of claim 1, wherein the HSC are CD34<sup>+</sup>.

15. (Currently Amended): The method of claim 1, wherein the genetically modified cells are provided to the patient about the time when the thymus begins to reactivate or shortly thereafter.

16. (Currently Amended): The method of claim 1, wherein ~~the method of~~ disrupting the sex steroid mediated signaling to the thymus is through administration of one or more pharmaceuticals.

17. (Currently Amended): The method of claim ~~[[11]]~~ 16, wherein the ~~pharmaceuticals~~ are pharmaceutical is selected from the group consisting of LHRH agonists, LHRH antagonists, anti-LHRH vaccines, and combinations thereof.

18. (Currently Amended): The method of claim ~~[[12]]~~ 17, wherein the LHRH agonists are selected from the group consisting of Goserelin, Leuprolide, Triptorelin, Meterelin, Buserelin, Histrelin, Nafarelin, Lutrelin, Leuprorelin, and Deslorelin.

19. (Currently Amended): A method for ~~preventing infection of a patient by HIV~~ reducing HIV viral titer or infection of new cells in a patient whose thymus has been at least in part deactivated, comprising the steps of ~~T-cell ablation~~

ablating the patient's T cells;[[,]]  
reactivating the thymus of the patient by ~~disruption of~~ disrupting sex steroid-  
mediated signaling to the thymus of the patient;[[,]] and  
administration of administering genetically modified cells to the patient,  
wherein the genetically modified cells are being selected from the group consisting of  
genetically modified HSC, lymphoid progenitor cells, myeloid progenitor cells, and  
combinations thereof, and the cells being genetically modified in vitro with a vector  
construct encoding and expressing a gene product that inhibits replication of human  
immunodeficiency virus (HIV).

20. (Currently Amended): The method of claim 19<sub>2</sub> wherein the genetically modified cells contain a stably expressible polynucleotide that prevents HIV infection of a T cell by HIV.

21. (Currently Amended): The method of claim 20<sub>2</sub> wherein the stably expressible polynucleotide is selected from the group consisting of a ~~nef~~ nef transcription factor gene, a gene that codes for a ribozyme that cuts HIV *tat* and/or *rev* genes, the trans-dominant mutant form of HIV-1 *rev* gene (RevM10), and an overexpression construct of the HIV-1 *rev*-responsive element (RRE), and functional fragments thereof.

22. (Currently Amended): The method of claim 19<sub>2</sub> wherein the HSC are CD34<sup>+</sup>.

23. (Currently Amended): The method of claim 19<sub>2</sub> wherein the genetically modified cells are ~~provided~~ administered to the patient about the time when the thymus begins to reactivate or shortly thereafter.

24. (Currently Amended): The method of claim 19, wherein the method of disrupting the sex steroid mediated signaling to the thymus is through administration of one or more pharmaceuticals.

25. (Currently Amended): The method of claim 24, wherein the ~~pharmaceuticals are~~ pharmaceutical is selected from the group consisting of LHRH agonists, LHRH antagonists, anti-LHRH vaccines, and combinations thereof.

26. (Currently Amended): The method of claim 25, wherein the LHRH agonists are selected from the group consisting of Goserelin, Leuprolide, Triptorelin, Meterelin, Buserelin, Histrelin, Nafarelin, Lutrelin, Leuprorelin, and Deslorelin.

27. (Currently Amended): A method for genetically altering a patient whose thymus has been at least in part deactivated, comprising:

reactivating the thymus of the patient by disrupting sex steroid-mediated signaling to the patient's thymus;

genetically modifying cells *in vitro* with a vector construct encoding and expressing a gene product that inhibits replication of human immunodeficiency virus (HIV); and

administering the genetically modified cells to the patient~~[[;]]~~, ~~wherein~~ the cells ~~are being~~ selected from the group consisting of stem cells, progenitor cells, and combinations thereof.

28. (Original): The method of claim 27, wherein the thymus of the patient has been at least in part atrophied before it is reactivated.

29. (Original): The method of claim 28, wherein the patient has a disease that at least in part atrophied the thymus of the patient.
30. (Original): The method of claim 28, wherein the patient has had a treatment of a disease that at least in part atrophied the thymus of the patient.
31. (Original): The method of claim 30, wherein the treatment is immunosuppression, chemotherapy or radiation treatment.
32. (Original): The method of claim 28, wherein the patient is post-pubertal.
33. (Original): The method of claim 27, wherein the stem cells are selected from the group consisting of hematopoietic stem cells, epithelial stem cells, and combinations thereof.
34. (Withdrawn): The method of claim 27, wherein the progenitor cells are selected from the group consisting of lymphoid progenitor cells, myeloid progenitor cells, and combinations thereof.
35. (Canceled)
36. (Original): The method of claim 33, wherein the cells are hematopoietic stem cells.
37. (Original): The method of claim 36, wherein the hematopoietic stem cells are CD34+.

38. (Original): The method of claim 36, wherein the hematopoietic stem cells are autologous.

39. (Original): The method of claim 36, wherein the hematopoietic stem cells are not autologous.

40. (Original): The method of claim 37, wherein the genetically modified hematopoietic stem cells are administered when the thymus begins to reactivate.

41. (Original): The method of claim 27, wherein the thymus is reactivated by disruption of sex steroid-mediated signaling to the thymus.

42. (Original): The method of claim 41, wherein the stem cells are selected from the group consisting of hematopoietic stem cells, epithelial stem cells, and combinations thereof.

43. (Withdrawn): The method of claim 41, wherein the progenitor cells are selected from the group consisting of lymphoid progenitor cells, myeloid progenitor cells, and combinations thereof.

44. (Canceled)

45. (Original): The method of claim 42, wherein the cells are hematopoietic stem cells.

46. (Original): The method of claim 45, wherein the genetically modified hematopoietic stem cells are administered at the time disruption of sex steroid-mediated signaling to the thymus is begun.

47. (Withdrawn): The method of claim 41, wherein the sex steroid-mediated signaling to the thymus is disrupted by surgical castration.

48. (Withdrawn): The method of claim 41, wherein the sex steroid-mediated signaling to the thymus is disrupted by chemical castration.

49. (Original): The method of claim 41, wherein the sex steroid-mediated signaling to the thymus is disrupted by administration of one or more pharmaceuticals.

50. (Previously Presented): The method of claim 49, wherein the one or more pharmaceuticals is selected from the group consisting of LHRH agonists, LHRH antagonists, anti-LHRH vaccines, anti-androgens, anti-estrogens, SERMs, SARMS, SPRMs, ERDs, aromatase inhibitors, anti-progestogens, and combinations thereof.

51. (Previously Presented): The method of claim 50, wherein the LHRH agonists are selected from the group selected from the group consisting of Goserelin, Leuprolide, Triptorelin, Meterelin, Buserelin, Histrelin, Nafarelin, Lutrelin, Leuprorelin, Deslorelin, Cystorelin, Decapeptyl, Gonadorelin, and combinations thereof.

52. (Withdrawn): The method of claim 50, wherein the LHRH antagonists are selected from the group consisting of Abarelix, Cetrorelix, and combinations thereof.



53. (Original): The method of claim 27, wherein the patient is infected with a virus.

54. (Original): The method of claim 53, wherein the virus is selected from the group consisting of Retroviridae, Picornaviridae, Calciviridae, Togaviridae, Flaviridae, Coronaviridae, Rhabdoviridae, Filoviridae, Paramyxoviridae, Orthomyxoviridae, Bungaviridae, Arenaviridae, Reoviridae, Birnaviridae, Hepadnaviridae, Parvoviridae, Papovaviridae, Adenoviridae, Herpesviridae, Poxviridae, and Iridoviridae.

55. (Original): The method of claim 27, wherein the patient is infected with a human immunodeficiency virus.

56-59. (Canceled)

60. (Original): The method of claim 27, further comprising ablating the T cells of the patient prior to reactivating the thymus and administering the genetically modified cells to the patient.

61. (Original): The method of claim 27, further comprising administering at least one cytokine, at least one growth factor, or a combination of at least one cytokine and at least one growth factor to the patient.

62. (Previously Presented): The method of claim 61, wherein the cytokine is selected from the group consisting of Interleukin 2 (IL-2), Interleukin 3 (IL-3), Interleukin 4 (IL-4), Interleukin 5 (IL-5), Interleukin 6 (IL-6), Interleukin 7 (IL-7), Interleukin 10 (IL-10),

Interleukin 12 (IL-12), Interleukin 15 (IL-15), Interferon- $\gamma$  (IFN- $\gamma$ ), and combinations thereof.

63. (Withdrawn): The method of claim 61, wherein the growth factor is selected from the group consisting of members of the epithelial growth factor family, members of the fibroblast growth factor family, stem cell factor, granulocyte colony stimulating factor (G-CSF), keratinocyte growth factor (KGF), and combinations thereof.

64-69. (Canceled)

70. (Currently Amended): The method of claim [[65]] 19, further comprising treating the patient with anti-retroviral therapy.

71. (Original): The method of claim 70, wherein the anti-retroviral therapy is Highly Active Retroviral Therapy (HAART).

72-80. (Canceled)

81. (Withdrawn): A method for enhancing transplantation of donor hematopoietic stem cells into the thymus of a recipient patient, comprising:

depleting the T cells of the patient,

reactivating the thymus of the patient; and

transplanting donor hematopoietic stem cells to the patient,

wherein uptake of the donor hematopoietic stem cells into the patient's thymus is enhanced as compared to the uptake that would have otherwise occurred in a patient prior to thymus reactivation.

82. (Canceled)

83. (Currently Amended): A method for improving uptake by the thymus of a patient of genetically modified cells or exogenous cells, comprising:

(a) reactivating the thymus of the patient by disrupting sex-steroid signaling to the thymus of the patient; and

(b) administering the genetically modified or exogenous cells to the patient,

~~wherein~~ the reactivated thymus of the patient ~~facilitates~~ facilitating improved uptake of genetically modified or exogenous cells by the thymus compared to the uptake of genetically modified or exogenous cells by the thymus of a patient that has not been reactivated.

84. (Withdrawn): A method for treating a T cell disease or disorder in a patient, comprising:

(a) reactivating the thymus of the patient; and

(b) administering genetically modified cells to the patient, wherein the genetically modified cells have been genetically modified to express a normal version of a defective gene that exists in the patient,

wherein the genetically modified cells are taken up by the reactivated thymus of the patient, and wherein the genetically modified cells or their progeny treats the T cell disease or disorder in the patient.

85. (Canceled)

86. (Withdrawn): A method for treating a patient with a genetic defect in a T cell or dendritic cell, comprising:

- (a) reactivating the thymus of the patient; and
- (b) administering autologous HSC that have been genetically modified to correct the genetic defect in the T cell or dendritic cell of the patient,

wherein the genetically modified HSC differentiate into T cells or dendritic cells expressing the normal gene in the reactivated thymus of the patient.

87. (Previously Presented): The method of claim 41, wherein the sex steroid-mediated signaling to the thymus is disrupted by lowering the level of a sex steroid hormone.

88. (Previously Presented): The method of claim 27, further comprising immunosuppressing the patient.